REMARKS / ARGUMENTS

Amendments to the Claims

Claims 1 through 20 are pending in the Application, however, claims 6 through 19 are withdrawn from consideration as being drawn towards a non-elected invention. Claims 1 through 3, and claim 20 are being amended as shown above. Claim 3 is being amended merely to correct a typographic error. Claims 1 and 19 are being amended to remove the phrase "that are potentially" to better reflect the utility of the invention. Claim 1 is being amended to better define the invention. Claim 2 is being amended to address a subset of biological activities related to focal adhesion kinase 2 function identified in claim 1, and no longer includes the binding of a second protein by focal adhesion kinase 2. Claim 20 is being amended to change its dependency to amended claim 1.

Applicants submit that these amendments, which do not add new matter to the application, are supported by the as-filed specification. Applicants respectfully request that these amendments be entered into the record, and further request reconsideration of the Application and examination of the amended claims in view of the remarks and arguments provided below.

SEQUENCE LISTING COMPLIANCE

The Office Action (in section 2, on page 3) alleges that the instant Application fails to comply with the requirements of 37 § CFR 1.821 through 1.825 because no sequence identification has been provided for the nucleic acids depicted in Figures 1 to 59 of the instant application.

In response, Applicants respectfully note that MPEP § 2422.02 specifically provides the following relevant passage:

> In view of the fact that many significant sequence characteristics may only be demonstrated by a figure, **the exclusive conformance requirement of this section may be relaxed for drawing figures**. This is especially true in view of the fact that **the representation of double stranded nucleotides is not permitted in the "Sequence Listing" and many significant nucleotide features, such as "sticky ends" and the like, will only be shown effectively by reference to a drawing figure.**

MPEP, Original 8th Edition, August 2001, § 2422.02, pages 2400-33 and 2400-34; emphasis added.

Applicants further note that Figures 1 through 59 depict siRNA molecules specifically designed to be targeted towards particular target sequences in fifty-nine different mRNAs encoding specific proteins whose cellular concentrations are to be lowered by RNA interference. As such, the Figures depict important structural features of the siRNAs (i.e., the required double-stranded character and the 3' overhangs of two deoxythymidine nucleotides each) that cannot be adequately demonstrated through a simple sequence listing. In view of this, and in further view of the fact that the depicted siRNA molecules are not the subject of the claims under examination, and the sequences of the individual strands of the double-stranded siRNAs need not be searched by the Examiner, Applicants respectfully request that the conformance requirements of 37 CFR § 1.821(b) be relaxed for those polynucleotides depicted in drawing Figures 1 through 59.

CLAIM OBJECTION

Claim 3 has been amended to correct the typographic error pointed out by the Examiner in the Office Action (in section 3, on page 3), thereby obviating the objection.

CLAIM REJECTIONS

Rejections Under 35 USC § 101 – Utility:

Claims 1-5 and 20 stand rejected under 35 USC § 101, because the claimed invention allegedly lacks an apparent or disclosed specific and substantial credible utility. Applicants respectfully traverse this rejection.

According to the Office Action (page 4): "The instant application does not disclose specific significance of biological activity of FAK2 with respect to Alzheimer's disease." Specifically, the Office Action of February 24, 2006 alleges:

> "The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that ... FAK2 is specifically associated

> with Alzheimer's disease or any other "neurological disorders, ailments and diseases." (p. 6, ll. 7-10)
>
> "The record does not support Applicant's claim that an agent that is capable to affect [an] activity of FAK2 would be beneficial in treatment of Alzheimer's disease." (p. 6, l. 21 – p. 7, l. 1)

Contrary to these allegations, Applicants note, as a first matter, the goal of the experiments described in the instant specification was to identify protein-protein interactions and proteins involved in neurological disorders and diseases, e.g., Alzheimer's disease, and biological processes associated with the pathological progression of these disorders and disease, such as neuronal death/amyloid precursor metabolism. *See*, generally, the Summary of Invention, from pages 3 through 11, and specifically, the "Biological Significance" section, at page 56. As noted in the "Biological Significance" section, changes in amyloid precursor metabolism are associated with Alzheimer's disease and neuronal death associated with Alzheimer's disease. As is also indicated throughout the specification, neuronal death is central to the pathogenesis of Alzheimer's disease.

As a second matter, Applicants note that the instant specification provides the following specific teachings on page 154:

> "Importantly, it has been discovered using the cell-based Aβ secretion assay disclosed in Example 8, below, that modulation of levels of expression of several of the interacting proteins of the instant invention affects the processing of APP, the production of Aβ in general, and the secretion of the neurotoxic Aβ_{42} peptide, in particular. Specifically, it has been discovered that overexpression of FAK2, SCD, CIB, and BAT3 results in increased secretion of Aβ_{42} in the cell based assay of Example 8. Consequently, it is expected that inhibition of FAK2, SCD, CIB, and BAT3, or a reduction in their expression, will result in decreased Aβ_{42} secretion. (This hypothesis has been tested and confirmed in the case of SCD.) Additionally, using the schemes described above, inhibitors of FAK2, SCD, CIB, and BAT3 can be selected and these selected inhibitors can be further tested for their ability to reduce Aβ_{42} secretion in the cell-based assay described in Example 8. The inhibitors so discovered can be subjected to iterative rounds of SAR, as described above, and the modified compounds can be further tested for their ability to more effectively reduce Aβ_{42} secretion. The compounds with the most desirable features can then be tested in subsequent pre-clinical trials in animals, before ultimately being tested in clinical trials in human patients in need of such treatment."

Applicants respectfully submit that this passage indicates that in cell-based assays, overexpression of FAK2 had been found to lead to increased amounts of the neurotoxic $A\beta_{42}$ peptide being secreted from cells. This passage also logically asserts that inhibition of FAK2, or a reduction in its expression, will result in decreased amounts of $A\beta_{42}$ being secreted.

In further support of these assertions, Applicants provide herewith a declaration under 37 C.F.R. § 1.132 from Dr. Paul L. Bartel. This declaration

- confirms the result disclosed above, that overexpression of FAK2 leads to increased amounts of the neurotoxic $A\beta_{42}$ peptide (and $A\beta_{40}$ peptide) being secreted from transformed cells in culture;
- further discloses that overexpression of a recombinant, catalytically-dead, dominant-negative "K457A" mutant form of FAK2 results in a statistically significant decrease in $A\beta_{40}$ and $A\beta_{42}$ being secreted from human cells in culture;
- asserts that these results suggest that inhibition of FAK2 within human cells in vivo, or a lowering of its concentration within such cells, would result in a reduction of the amount of $A\beta_{40}$ and $A\beta_{42}$ secreted by such cells; and
- concludes that, therefore, inhibition of FAK2 should have therapeutic utility.

Importantly, the Bartel declaration shows that (a) increased levels of FAK2 results in an increase in secreted amyloid beta peptides, and (b) expression of a dominant negative mutant form of FAK2 results in a decrease in secreted amyloid beta peptides. Applicants note that increased amyloid beta peptide secretion, particularly of $A\beta_{42}$, is considered a pathological hallmark of Alzheimer's disease. Thus, the inventors have identified a novel association between FAK2 activity and Alzheimer's disease pathoetiology.

It is respectfully submitted that the Bartel declaration provides clear support for the credibility of the asserted "real world" use for the claimed method of identifying agents useful for the treatment of Alzheimer's disease.

In view of the Bartel declaration, and the teachings of the specification discussed above, Applicants respectfully request withdrawal of the utility rejection.

Rejections Under 35 USC § 112, 1st Paragraph – Enablement:

Claims 1-5 and 20 stand rejected under 35 USC § 112, 1st paragraph, because the claimed invention allegedly is not supported by either a clear asserted utility or a well-established utility.

With respect to this aspect of the Enablement Rejection, Applicants respectfully submit that the factors related to the utility rejection under 35 USC § 101, which necessitated the enablement rejection under 35 USC § 112, 1st paragraph, have been adequately addressed in the discussions above, and in the declaration under 37 CRF § 1.132 provided. In view of these teachings, Applicants respectfully request that this aspect of the enablement requirement, for alleged lack of utility, be rescinded.

Claims 1-5 and 20 also stand rejected under 35 USC § 112, 1st paragraph, as allegedly being "single means claims." Applicants have amended claim 1 to require that said test agent **inhibit** the biological activity related to focal adhesion kinase 2 function, thereby obviating the rejection.

In view of the arguments and amendment provided above, Applicants respectfully submit that the claimed invention is supported by an adequately enabling specification, therefore Applicants respectfully request the withdrawal of the enablement rejections under 35 USC § 112, 1st paragraph.

Rejections Under 35 USC § 112, 1st Paragraph – Written Description:

Claims 2 and 20 stand rejected under 35 USC § 112, 1st paragraph, as containing subject matter allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Office Action observes that claim 2, and claim 20, which is dependent therefrom, are directed to methods using "fragments and homologues of FAK2" and that these claims "do not require that the recited fragments and homologues possess any particular conserved structure or other disclosed." (Office Action, section 8, page 8).

In response, Applicants have amended claim 1 to recite a first protein, which is (a) full-length focal adhesion kinase 2; (b) a polypeptide that has an amino acid sequence at least about 75% identical to focal adhesion kinase 2 that exhibits a biological activity

related to focal adhesion kinase 2 function; or (c) a fragment of (a) or (b) that retains said biological activity. Applicants respectfully submit that focal adhesion kinase 2 is a protein that was well known in the art at the time the instant application was filed, and that the amended claims are supported by a specification that provides adequate description for said first protein because the claims refer to a particular conserved structure (the amino acid sequence of focal adhesion kinase 2 and fragments thereof, as well as amino acid sequences at least 75% identical thereto), and a functional limitation (that said first protein must bind to said second protein).

In view of these arguments and the amendments provided, Applicants respectfully submit that the claimed invention is supported by a specification with adequate written description, therefore Applicants respectfully request the withdrawal of the written description rejection under 35 USC § 112, 1st paragraph.

Rejections Under 35 USC § 112, 2nd Paragraph – Indefiniteness:

Claims 2 and 20 stand rejected under 35 USC § 112, 2nd paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that the limitation "a protein that interacts with focal adhesion kinase 2" in the original claim 2 lacks antecedent basis in claim 1. Further, claim 20 is rejected as being indefinite for being dependent from original claim 2.

Applicants have amended claim 1 to recite the "ability to bind a second protein," and have deleted the recitation of a second protein from claim 2, thereby obviating the alleged improper antecedent basis rejection. Applicants have also amended claim 20 to be dependent upon claim 1 (instead of claim 2), and provide (in claim 20) examples of three species of "second proteins" that focal adhesion kinase 2 can bind. Applicants respectfully submit that in claim 1, the phrase "second protein" represents a genus of proteins, which comprises, e.g., the species disclosed in claim 20. Applicants further submit that claim 1 is definite, by virtue of the fact that one of skill in the art would understand exactly what is meant by the phrase "wherein said biological activity is ... the ability to bind a second protein" and that to limit the genus of "second proteins" in claim

1 to individual species would unnecessarily narrow the scope of the claims beyond that which the applicant regards as the invention.

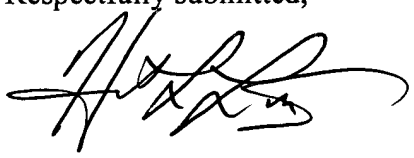
In view of these amendments and arguments, Applicants respectfully request that the rejection under 35 USC § 112, 2nd paragraph, be withdrawn.

CONCLUSION

Applicants believe that once the amendments proposed above have been incorporated into the pending claims, and the arguments presented above are considered, the outstanding rejections will be withdrawn and the pending claims will be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Examiner determine that additional issues remain which might be resolved by a telephone conference, she is respectfully invited to contact the undersigned via his direct line (801-883-3463).

A petition for a two-month extension of time for the filing of this response is being filed concurrently herewith. Provisions for the payment of the necessary fee have been made in the petition. Therefore, it is believed that no other extension of time, or any additional fees are due with this response. If this is incorrect, an extension of time as deemed necessary is hereby requested, and the Commissioner is hereby authorized to charge any appropriate fees or deficiency or credit any over payment to Deposit Account no. **50-1627**.

Respectfully submitted,



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